

DR SIDDHARTHA DASH (Orcid ID : 0000-0003-0533-7465)

Article type : Letter to the Editor

Covid-19 vaccine induced Steven-Johnson syndrome: a case report

S. Dash, C.S. Sirka, S. Mishra and P. Viswan

Department of Dermatology, and Venereology, All India Institute of Medical Sciences (AIIMS),
Bhubaneswar, Odisha, India.

Corresponding author: Dr. Chandra Sekhar Sirka, M.D

Email: csirka2006@gmail.com

Conflict of interest: None to declare

Funding: None

Dear editor,

Steven-Johnson syndrome (SJS) is a severe cutaneous adverse drug reaction. Its occurrence due to vaccines is scant.¹ We report a case of SJS caused by COVID-19 vaccine in an adult.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/CED.14784](https://doi.org/10.1111/CED.14784)

This article is protected by copyright. All rights reserved

A 60-year-old male presented with complaints of fever, oral ulceration and skin rash three days after the first dose of COVID-19 vaccine, for which he visited a local physician and was prescribed paracetamol and levocetirizine, in spite of which the symptoms were not controlled and gradually the rashes became generalised in distribution. The patient presented to the emergency department after seven days of development of lesions, throughout which the fever was persisting. On cutaneous examination, there were multiple purpuric macules present all over the body with peri-lesional erythema. The lesions coalesced to form large sheets of necrosed skin over front and back of trunk, with few areas showing bullae. Mucosal involvement was present in the form of oral erosions, hemorrhagic crusting over the lips, eye congestion and erosions over the glans (Fig.1). Based on the course and morphology, SJS was suspected and a detailed drug history was elicited, which revealed the patient was on teneligliptin, metformin and amlodipine for diabetes and hypertension respectively since last six months. Rest of the drugs were prescribed after the patient developed fever and skin rash and the patient denied any other drug intake before development of symptoms. The SCORETEN revealed a score of one at the day of admission and the Naranjo algorithm revealed a causal association of two (possible association) between the vaccine and the adverse drug reaction. Histopathological examination from the erythematous lesion revealed orthokeratosis with epidermal atrophy, moderate intraepidermal infiltration of lymphocytes and neutrophils with moderate spongiosis, scattered degenerated apoptotic keratinocytes, patchy areas of basal cell degeneration and interface dermatitis and perivascular and peri-adnexal inflammatory cell infiltrate along with extravasation of erythrocytes in dermis (Fig. 2). A diagnosis of SJS was made and the patient was started on oral cyclosporine 300mg and the patient improved completely after seven days (Fig.S1), and patient was counselled to defer the 2nd dose of vaccine and was issued a drug card.

Diagnosis of SJS is made on the basis of clinical suspicion and histological findings. Suspicion of SJS arose due to the sudden appearance of erythematous, reticulate patches on skin, mucosal ulceration and constitutional symptoms. The diagnosis was confirmed by the presence of epidermal keratinocyte necrosis. Chahal et al. adopted similar diagnostic approach of SJS, which includes clinical findings, corroborative history and histopathological findings.¹ Naranjo algorithm score is widely used for assessing causal association in drug reaction.² The index case was a known diabetic and hypertensive, on teneligliptin, metformin and amlodipine. He had consumed antihypertensive drug and vaccine prior to development of SJS but the continued intake of the

antihypertensive drug did not aggravate the condition. The Naranjo scale score two in the patient suggested possible association of vaccine in development of SJS.

COVID-19 vaccine has two components (virotopes and excipients) and both can cause severe drug reaction.³ In the present case virotopes of the vaccine has been believed to cause SJS. Further, authors hypothesize that the expression of the virotopes “vaccine antigens” on the surface of keratinocytes, leads to a CD8+ T-lymphocyte response against epidermal cells and causes apoptosis of keratinocytes and detachment of dermo-epidermal junction leading to SJS in genetically susceptible individual.⁴ This is further supported by the ability of ChAdOx1 nCoV- 19 corona virus vaccine (Recombinant) to produce T-cell specific response, which is predominantly Th1 based, which may have induced immune response and keratinocyte cell damage.⁵ Further, in an extensive review we did not come across excipients like L-Histidine, L-Histidine HCL, Sucrose, Sodium Chloride, Magnesium Chloride, Polysorbate 80, EDTA (Edetate Disodium), Ethanol, and water causing severe delayed type hypersensitivity reactions like SJS.³

Hereby, to the best of our knowledge we are reporting the first case of COVID-19 vaccine induced SJS. However, this case illustrates an exceedingly rare complication of the vaccine and the benefits far outweighs the risk in the current scenario and should not create hesitancy among population for receiving vaccination.

References

1. Chahal D, Aleshin M, Turegano M, Chiu M, Worswick S. Vaccine-induced toxic epidermal necrolysis: A case and systematic review. *Dermatol Online J*. 2018 Jan 15;24(1):13030/qt7qn5268s.
2. Belhekar MN, Taur SR, Munshi RP. A study of agreement between the Naranjo algorithm and WHO-UMC criteria for causality assessment of adverse drug reactions. *Indian journal of pharmacology*. 2014 Jan;46(1):117.
3. Stone CA Jr, Rukasin CRF, Beachkofsky TM, Phillips EJ. Immune-mediated adverse reactions to vaccines. *Br J Clin Pharmacol*. 2019 Dec;85(12):2694-2706.
4. Chahal D, Aleshin M, Turegano M, Chiu M, Worswick S. Vaccine-induced toxic epidermal necrolysis: A case and systematic review. *Dermatol Online J*. 2018 Jan 15;24(1):13030/qt7qn5268s.

5. Ramasamy MN, Minassian AM, Ewer KJ, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial [published correction appears in Lancet. 2021 Dec 19;396(10267):1978] [published correction appears in Lancet. 2021 Apr 10;397(10282):1350]. Lancet. 2021;396(10267):1979-1993.

Figure Legends:

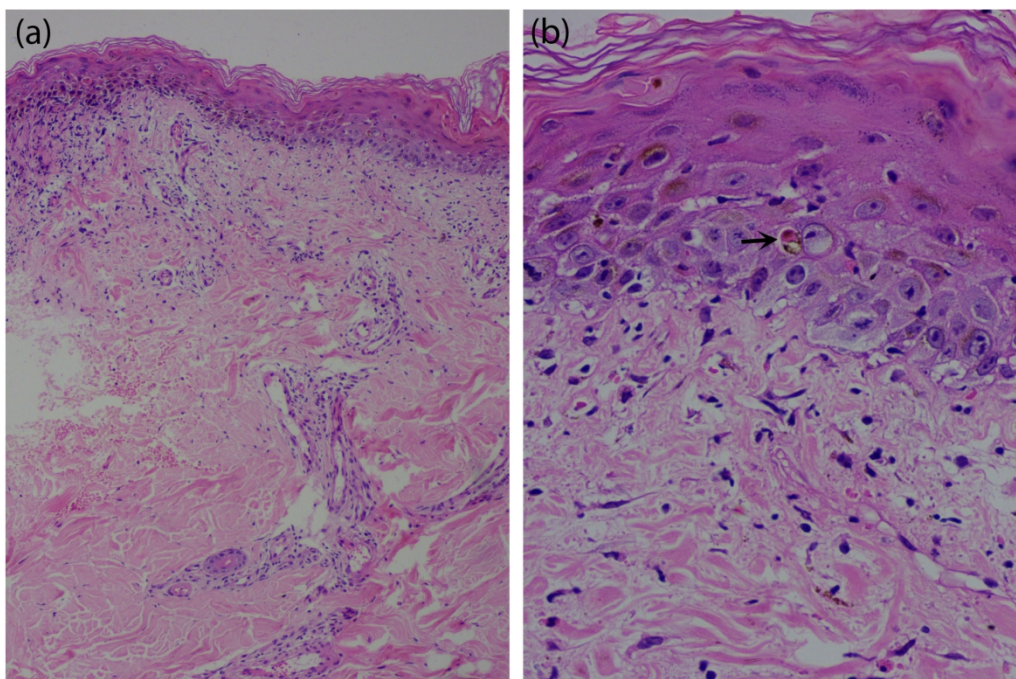
Figure1: (a) Large sheets of necrosed skin in front of trunk, with few areas showing bullae. (b) Involvement of face with erosions in palpebral conjunctiva and necrotic crusting over lips.

Figure 2: (a) Histopathology shows orthokeratosis with epidermal atrophy, scattered degenerated apoptotic keratinocytes, patchy areas of basal cell degeneration and interface dermatitis and perivascular and peri-adnexal inflammatory cell infiltrate along with extravasation of erythrocytes in dermis (H&E, X50). (b) Apoptotic keratinocytes (arrow) along with upper dermal edema and extravasation of erythrocytes (H&E, X400).

Figure S1: (a & b) Healed lesions after treatment.



ced_14784_f1.jpg



ced_14784_f2.jpg